REMARKS

Claims 1-30 are pending in this application. Claims 13-15 and 23-30 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1-12 and 16-22 are rejected. In view of the following remarks, reconsideration of claims 1-12 and 16-22 is respectfully requested.

§103 Rejections

Claims 1-4, 6-7, 16-17 and 19-20 are rejected under 35 U.S.C. §103(a) as being unpatentable over Golay et al. (Blood, vol 98, page 3383-9)(hereinafter "Golay"), in view of Hogan et al. (Cancer genet cytogenet, vol 110, page 77-81, 1999)(hereinafter "Hogan"), Fonseca et al. (Leukemia, vol 15, page 981-6, 2001)(hereinafter "Fonseca"), Witzig et al. (Leukemia and lymphoma, vol 14, page 447-451, 1993)(hereinafter "Witzig"), and Catovsky D (Hematol Cell Ther, vol 39, page S5-S11, 1997)(hereinafter "Catovsky").

Applicant submits that the cited references, alone or in combination, do not teach or suggest every feature as recited in independent claims 1 and 16. In particular, they do not teach or suggest, alone or in combination, that the presence of 17q13.1 deletions indicate that a patient would be refractory to treatment with a therapeutic agent that specifically binds to CD20 antigens on the surface of B-lymphocytes. Moreover, they do not teach or suggest that the presence of 17q13.1 deletions and one or more of the 13q14.3, 11q22-q23, and trisomy 12 abnormalities indicates that a patient will be responsive to treatment with a therapeutic agent that specifically binds to CD20 antigens on the surface of B-lymphocytes.

Golay is concerned with the mechanism of action of rituximab and recites that CD20 levels correlate with response to rituximab. Golay is not concerned with 17q13.1, 13q14.3, 11q22-q23, or trisomy 12 chromosomal abnormalities. Nowhere does Golay suggest that the presence of 17q13.1 deletions indicate that a patient would be refractory to treatment with a therapeutic agent that specifically binds to CD20 antigens on the surface of B-lymphocytes. Nowhere does Golay et al. suggest that 17q13.1 deletions and one or more of the 13q14.3, 11q22-q23, and trisomy 12 abnormalities indicates that a patient will be responsive to treatment

with a therapeutic agent that specifically binds to CD20 antigens on the surface of B-lymphocytes.

Hogan does not provide what Golay lacks. Hogan is concerned with screening patients for CLL based upon the presence of CD5+ CD20+ B cells. Hogan is not concerned with levels of CD20+ or correlating CD20+ levels with chromosomal abnormalities. Nowhere does Hogan teach or suggest any correlation between CD20+ levels and 13q14 deletions or trisomy 12. Hogan does not teach or suggest any correlation between 13q14 deletions or trisomy 12 and treatment with a therapeutic agent that binds to CD20 antigens on the surface of B-lymphocytes.

Fonseca does not provide what Golay and Hogan lack. Fonseca describes probes for chromosome 13. Fonseca does not teach or suggest that the presence of 17q13.1 deletions indicate that a patient would be refractory to treatment with a therapeutic agent that specifically binds to CD20 antigens on the surface of B-lymphocytes. Moreover, Fonseca does not teach or suggest that the presence of 17q13.1 deletions and one or more of the 13q14.3, 11q22-q23, and trisomy 12 abnormalities indicates that a patient will be responsive to treatment with a therapeutic agent that specifically binds to CD20 antigens on the surface of B-lymphocytes.

Witzig does not provide what the above references lack. Witzig describes a correlation between trisomy 12 and CD20 antigen expression. Witzig does not teach or suggest that the presence of the 17q13.1 deletion and trisomy 12 indicate that a patient will be responsive to treatment with a therapeutic agent that specifically binds to CD20 antigens on the surface of B-lymphocytes. Witzig does not teach or suggest that the presence of 17q13.1 deletions indicate that a patient would be refractory to treatment with a therapeutic agent that specifically binds to CD20 antigens on the surface of B-lymphocytes.

Catovsky does not provide what the above references lack. Catovsky recites that patients with 17q13.1 deletions frequently fail to respond to therapy. Nowhere does Catovsky specify the type of therapy. Current therapies used to treat B-cell CLL include purine analogs, alkylating agents, and an anti-CD52 monoclonal antibody, which do not specifically bind to CD20 antigens on the surface of B-lymphocytes. Catovsky in no way suggests that patients fail to respond to treatment with a therapeutic agent that specifically binds to CD20 antigens on the surface of B-lymphocytes. Quite simply, Catovsky does not teach or suggest that 17q13.1 deletions are indicative that a patient would be refractory to treatment with a therapeutic agent that specifically

binds to CD20 antigens on the surface of B-lymphocytes.

Therefore, even if combined, Golay, Hogan, Fonseca, Witzig, and Catovsky, do not provide the methods recited in instant claims 1-4, 6-7, 16-17, and 19-20. Accordingly, Applicants submit that the rejection of these claims be withdrawn.

Claims 1-8 and 16-22 are rejected under 35 U.S.C. §103(a) as being unpatentable over Golay, Catovsky, Hogan, and Witzig, further in view of Morrison (US Patent Application Publication, US 2003/0087248, effective filing date Feb. 20, 2001) (hereinafter "Morrison") and Stilgenbauer et al. (Blood, vol 94, page 3262-4, 1999)(hereinafter "Stilgenbauer").

As outlined above, Golay, Catovsky, Hogan, and Witzig, alone or in combination, do not teach or suggest every feature as recited in independent claims 1 and 16. In particular, they do not teach or suggest, alone or in combination, that the presence of 17q13.1 deletions are indicative that a patient would be refractory to treatment with a therapeutic agent that specifically binds to CD20 antigens on the surface of B-lymphocytes. Moreover, they do not teach or suggest that the presence of 17q13.1 deletions and one or more of the 13q14.3, 11q22-q23, and trisomy 12 abnormalities indicate that a patient will be responsive to treatment with a therapeutic agent that specifically binds to CD20 antigens on the surface of B-lymphocytes.

Morrison and Stilgenbauer do not provide what Golay, Catovsky, Hogan, and Witzig lack. Morrison is concerned with using chromosomal probes to detect cancer. Stilgenbauer is concerned with using chromosomal probes to detect chromosomal deletions in mantle cell lymphoma. Neither Morrison nor Stilgenbauer, alone or in combination, are concerned with predicting the response of a patient with CLL to treatment with a therapeutic agent that specifically binds to CD20 antigens on the surface of B-lymphocytes. They do not teach or suggest, alone or in combination, that the presence of 17q13.1 deletions are indicative that a patient would be refractory to treatment with a therapeutic agent that specifically binds to CD20 antigens on the surface of B-lymphocytes. And they do not teach or suggest that the presence of 17q13.1 deletions and the presence of one or more of the 13q14.3, 11q22-q23, and trisomy 12 abnormalities would indicate that the patient will be responsive to treatment with a therapeutic agent that specifically binds to CD20 antigens on the surface of B-lymphocytes.

Therefore, even if combined, Golay, Catovsky, Hogan, Witzig, Morrison, and

Stilgenbauer do not provide the methods recited in instant claims 1-8 and 16-22. Accordingly, Applicants submit that the rejection of these claims be withdrawn.

Claims 9-12 are rejected under 35 U.S.C. §103(a) as being unpatentable over Morrison, in view of Fonseca et al. and Stilgenbauer et al., and Croce et al. (US Patent, 5928884)(hereinafter "Croce").

Applicant submits that the cited references, alone or in combination, do not teach or suggest every feature as recited in independent claim 9. They do not teach or suggest, alone or in combination, a diagnostic kit for determining the chemosensitivity of a chronic lymphocytic leukemia patient to treatment with a therapeutic agent that is specific for CD20+ B lymphocytes.

Morrison does not teach or suggest a diagnostic kit for determining the chemosensitivity of a chronic lymphocytic leukemia patients to any type of treatment, let alone to treatment with a therapeutic agent that is specific for CD20+ B lymphocytes. Morrison is concerned with using chromosomal probes to detect cancer. Morrison does not suggest that its methods or probes can be used to determine the chemosensitivity of a chronic lymphocytic leukemia patient to treatment with a therapeutic agent that is specific for CD20+ B lymphocytes. Neither Fonseca, Stilgenbauer, nor Croce provide what Morrison lacks. In contrast to Morrison, Stilgenbauer is concerned with using chromosomal probes to detect chromosomal deletions in mantle cell lymphoma, while Croce is concerned with kits using tumor suppressor FHIT genes as diagnostic tools. Neither Fonseca, Stilgenbauer, nor Croce suggest a diagnostic kit for determining the chemosensitivity of a chronic lymphocytic leukemia patient to treatment with a therapeutic agent that is specific for CD20+ B lymphocytes. And even if combined, Morrison, Fonseca, Stilgenbauer, and Croce do not provide the methods recited in claims 9-12. Accordingly, applicants submit that the rejection of these claims be withdrawn.

CONCLUSION

In view of the above remarks, allowance of claims 1-12 and 16-22 is respectfully requested.

Respectfully submitted,

Date: August 15, 2006

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